

WHAT IS CLAIMED IS:

1. A method for producing an index indicative of brain disease comprising the steps of:

collecting positron emission tomographic image data showing metabolic activity in the brain of a patient;

spatially normalizing said image data using a standardized three dimensional coordinate system;

spatially filtering the normalized image data;

selecting specific regions of the brain showing extremes in metabolic activity;

collecting mean intensity values for the normalized, filtered image data from said selected specific brain regions;

weighting said mean intensity values with standard weights derived from the group analysis used to create the standard; and

normalizing the ratio of said mean, weighted, metabolic activity image data to produce a numerical index.

2. The method according to claim 1 wherein the metabolic activity is indicated by glucose metabolism of brain cells.

3. The method according to claim 1 wherein the three-dimensional coordinate system is Talairach space.

4. The method according to claim 3 wherein the image data is transformed to conform in Talairach space using a twelve parameter, linear, affine algorithm.

5. The method according to claim 1 wherein the transformed image data is filtered using an eight millimeter, isotropic, Gaussian filter kernel.

6. The method according to claim 1 wherein said normalized, filtered image data is compared to data from age-matched patient controls using Standard Parametric Mapping techniques in a statistical group comparison.

7. The method according to claim 6 wherein the Standard Parametric Mapping is used to generate a map of the brain and the map is converted to a unit normal distribution Z score.

8. The method according to claim 7 wherein the Standard Parametric Mapping Z-score results are utilized to select specific regions of the brain showing extremes in metabolic activity.

9. The method according to claim 1 wherein statistical mapping procedures are utilized to create a plurality of three dimensional, identically sized, spherical volumes of interest.

10. The method according to claim 9 wherein mean intensity values for the volume elements are contained within each of said volumes of interest are determined wherein each said volume element is a cube of selected dimension.

11. The method according to claim 9 wherein each of a plurality of volumes of interest is placed at specific coordinates in said three dimensional coordinate system.

12. The method according to claim 9 wherein two sets of volumes of interest are selected, the first set being comprised of a plurality of volumes of interest with increased metabolism and the second set being comprised of a plurality of volumes of interest with decreased metabolism.

13. The method according to claim 12 wherein said first set of volumes of interest comprises four volumes of interest with increased metabolism and said second set of volumes of interest comprises five volumes of interest with decreased metabolism.

14. The method according to claim 13 wherein said volumes of interest with increased metabolism comprise the vermis, motor, R pons and cerebellar nuclei, and where said volumes of interest with decreased metabolism comprise the posterior cingulate, L parietal, R parietal01 temporal01, and temporal02.

15. The method according to claim 12 additionally comprising;

normalizing the intensity data of said volumes of interest, said mean normalization comprising dividing each intensity value from each volume of interest by the average of the values of said intensities thereby establishing a mean value of one (1) for each subject's data set ;

dividing the data sets into evenly valued subgroups with designation of c_i for the i^{th} control subgroup and p_i for the i^{th} patient subgroup;

forming mixed groups by pairing controls with patients to yield small data sets for use in training an artificial neural network;

rescaling said small data sets to appropriately match the input range of said data sets to the range of an output transfer function;

utilizing said rescaled output from said transfer function as inputs for training an artificial neural network to produce the neural network cognitive decline index (CDInn); and

testing said CDInn on the full data set to assess the classification accuracy of said CDInn.

16. The method according to claim 15 wherein said output transfer function comprises a linear function.

17. The method according to claim 15 additionally comprising utilizing the outputs from said transfer function as inputs for a second output transfer function.

18. The method according to claim 15 wherein said output transfer function comprises a linear function and said second output transfer function comprises a tangent sigmoidal transfer function.

19. The method according to claim 12 wherein said first set of volumes of interest comprises four volumes of interest with increased metabolism and said second set of volumes of interest comprises nine volumes of interest with decreased metabolism.

20. The method according to claim 12 wherein the intensity values of said volumes of interest are used to create a first and second data set, said first data set comprising the ratios of the mean value of the intensities of the first set of volumes of interest with increased metabolism divided by the intensity values of each of the volumes of the second set of volumes of interest with decreased metabolism and said second data set comprising the ratios of each of the intensity values of the first set of volumes of interest with increased metabolism divided by the mean value of the intensities of the second set of volumes of interest with decreased metabolism.

21. The method according to claim 15 wherein the intensity values of the set of said thirteen volumes of interest are used to create a third and fourth data set, said third data set comprising the ratios of the mean of the intensity value of the set of four volumes of interest with increased metabolism divided by the intensity values of

each of the nine volumes of interest with decreased metabolic activity and the fourth data set comprising the ratio of each of the intensity values of the set of four volumes of interest of increased metabolic activity divided by the mean value of the intensities of the volumes of interest with increased metabolic activity.

22. The method according to claim 1 wherein the disease detected is one or more of the following diseases:

- Alzheimer's disease;
- Parkinson's disease;
- Huntington's disease;
- Pick's Dementia;
- dementia with Lewy bodies;
- disease resulting from head injury;
- disease resulting from patient intake of drugs; and
- disease resulting from patient intake of alcohol.

23. The method according to claim 1 additionally comprising

- using said weighted intensity values as a baseline reference for iterative optimization of each weighted intensity value;
- forming a subset of weights taken from a control subject database said control subjects forming a first group;
- maximally separating each of said weighted intensity values of each region taken from said patient from intensity values of analogous regions taken from control subjects using a dynamic table of patient weights and control subject weights wherein separations in intensity values between the patients and the normal controls are assessable in real time;
- merging patient data with data from previous patients in a patient database to constitute a second group;
- iteratively adjusting said weighted intensity values to maximize the separation between said patient and said control subjects while minimizing within-group variance; and
- calculating a second Cognitive Decline Index utilizing the optimized weighted intensity values.

24. A method for diagnosing degenerative brain disease comprising the steps of:

collecting positron emission tomographic image data showing metabolic activity of a brain of a patient;

spatially normalizing said image data using a three dimensional coordinate system;

smoothing said normalized image data;

applying objective statistical analysis to select specific regions of the brain, said regions showing extreme changes in metabolic activity;

collecting mean intensity values for said normalized, smoothed image data from said selected specific regions;

weighting said mean intensity values based on a comparison of said mean intensity values taken from said patient to a set of mean intensity values of said specific brain region taken from a normal patient population; and

calculating an index using said weighted, mean intensity values wherein said index is a normalized ratio of said weighted, mean intensity values, taken from said sampled regions.

25. Apparatus for producing an index indicative of brain pathology resulting from injury, disease, or other cause comprising:

a positron emission tomographic scanner; and

a computer operatively connected to the outputs of said PET scanner, said computer being programmed to calculate an index indicative of brain disease by:

collecting positron emission tomographic image data showing metabolic activity in the brain of a patient;

spatially normalizing said image data using a standardized three dimensional coordinate system;

spatially filtering the normalized image data;

selecting specific regions of the brain showing extremes in metabolic activity;

collecting mean intensity values for the normalized, filtered image data from said selected specific brain regions;

weighting said mean intensity values with standard weights derived from the group analysis used to create the standard; and
normalizing the ratio of said mean, weighted, metabolic activity image data to produce a numerical index.

26. The apparatus according to claim 25 wherein the metabolic activity is indicated by glucose metabolism of brain cells.

27. The apparatus according to claim 25 wherein the three-dimensional coordinate system is Talairach space.

28. The apparatus according to claim 27 wherein the image data is transformed to conform in Talairach space using a twelve parameter, linear, affine algorithm.

29. The apparatus according to claim 25 wherein the transformed image data is filtered using an eight millimeter, isotropic, Gaussian filter kernel.

30. The apparatus according to claim 25 wherein said normalized, filtered image data is compared to data from age-matched patient controls using Standard Parametric Mapping techniques in a statistical group comparison.

31. The apparatus according to claim 30 wherein the Standard Parametric Mapping is used to generate a map of the brain and the map is converted to a unit normal distribution Z score.

32. The apparatus according to claim 31 wherein the Standard Parametric Mapping Z-score results are utilized to select specific regions of the brain showing extremes in metabolic activity.

33. The apparatus according to claim 25 wherein statistical mapping procedures are utilized to create a plurality of three dimensional, identically sized, spherical volumes of interest.

34. The apparatus according to claim 33 wherein mean intensity values for the volume elements are contained within each of said volumes of interest are determined wherein each said volume element is a cube of selected dimension.

35. The apparatus according to claim 33 wherein each of a plurality of volumes of interest is placed at specific coordinates in said three dimensional coordinate system.

36. The apparatus according to claim 33 wherein two sets of volumes of interest are selected, the first set being comprised of a plurality of volumes of interest with increased metabolism and the second set being comprised of a plurality of volumes of interest with decreased metabolism.

37. The apparatus according to claim 36 wherein said first set of volumes of interest comprises four volumes of interest with increased metabolism and said second set of volumes of interest comprises five volumes of interest with decreased metabolism.

38. The apparatus according to claim 17 wherein said volumes of interest with increased metabolism comprise the vermis, motor, R pons and cerebellar nuclei and where said volumes of interest with decreased metabolism comprise the posterior cingulate, L parietal, R parietal01 temporal01, and temporal02.

39. The apparatus according to claim 36 additionally comprising;

normalizing the intensity data of said volumes of interest, said mean normalization comprising dividing each intensity value from each volume of interest by the average of the values of said intensities thereby establishing a mean value of one (1) for each subject's data set ;

dividing the data sets into evenly valued subgroups with a designation of c_i for the i^{th} control subgroup and p_i for the i^{th} patient subgroup;

forming mixed groups by pairing controls with patients to yield small data sets for use in training an artificial neural network;

rescaling said small data sets to appropriately match the input range of said data sets to the range of an output transfer function;

utilizing said rescaled output from said transfer function as inputs for training an artificial neural network to produce the neural network cognitive decline index (CDInn); and

testing said CDInn on the full data set to assess the classification accuracy of said CDInn.

40. The apparatus according to claim 39 wherein said output transfer function comprises a linear function.

41. The apparatus according to claim 39 additionally comprising utilizing the outputs from said transfer function as inputs for a second output transfer function.

42. The apparatus according to claim 39 wherein said output transfer function comprises a linear function and said second output transfer function comprises a tangent sigmoidal transfer function.

43. The apparatus according to claim 36 wherein said first set of volumes of interest comprises four volumes of interest with increased metabolism and said second set of volumes of interest comprises nine volumes of interest with decreased metabolism.

44. The apparatus according to claim 36 wherein the intensity values of said volumes of interest are used to create a first and second data set, said first data set comprising the ratios of the mean value of the intensities of the first set of volumes of interest with increased metabolism divided by the intensity values of each of the volumes of the second set of volumes of interest with decreased metabolism and said second data set comprising the ratios of each of the intensity values of the first set of volumes of interest with increased metabolism divided by the mean value of the intensities of the second set of volumes of interest with decreased metabolism.

45. The apparatus according to claim 39 wherein the intensity values of the set of said thirteen volumes of interest are used to create a third and fourth data set, said third data set comprising the ratios of the mean of the intensity value of the set of four volumes of interest with increased metabolism divided by the intensity values of each of the nine volumes of interest with decreased metabolic activity and the fourth data set comprising the ratio of each of the intensity values of the set of four volumes of interest of increased metabolic activity divided by the mean value of the intensities of the volumes of interest with increased metabolic activity.

46. A program storage device operable for producing an index indicative of brain pathology resulting from injury, disease, or other cause comprising computer program language for:

collecting positron emission tomographic image data showing metabolic activity in the brain of a patient;

spatially normalizing said image data using a standardized three dimensional coordinate system;

spatially filtering the normalized image data;

selecting specific regions of the brain showing extremes in metabolic activity;

collecting mean intensity values for the normalized, filtered image data from said selected specific brain regions;

weighting said mean intensity values with standard weights derived from the group analysis used to create the standard; and

normalizing the ratio of said mean, weighted, metabolic activity image data to produce a numerical index.

47. A method for monitoring the effectiveness of treatment of cognitive impairment utilizing an index indicative of brain disease comprising the steps of:

(a) collecting positron emission tomographic image data showing metabolic activity in the brain of a patient;

(b) spatially normalizing said image data using a standardized three dimensional coordinate system;

(c) spatially filtering the normalized image data;

(d) selecting specific regions of the brain showing extremes in metabolic activity;

(e) collecting mean intensity values for the normalized, filtered image data from said selected specific brain regions;

(f) weighting said mean intensity values with standard weights derived from the group analysis used to create the standard;

(g) normalizing the ratio of said mean, weighted, metabolic activity image data to produce a numerical index;

(h) administering a treatment for cognitive impairment;

(i) repeating steps (a) – (g); and

(j) changing the method of treatment depending upon the numerical index.